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PATENT TRADEMARK OFFICE

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1645
R. Judd et al.	) Examiner: S. Devi
Appln. No. 09/994,192	)
Filed: November 26, 2001	)
For: OMP85 PROTEINS OF NEISSERIA GONORRHOEAE AND NEISSERIA MENINGITIDIS, COMPOSITIONS CONTAINING SAME AND METHODS	)

Commissioner for Patents
Washington, DC 20231

DECLARATION UNDER 37 CFR § 1.132

Sir:

I, Ralph C. Judd, residing at 316 Wickiup, Florence, Montana, 59833, a citizen of the United States of America, do declare and state that:

1.   I am one of the named joint inventors of the subject matter claimed in the above-identified patent application

2.   This Declaration is submitted in the above-identified application in response to the Examiner's rejection under 35 USC § 112, first paragraph in the Office Action dated July 17, 2002. The following information is provided to demonstrate that the isolated polypeptide of SEQ ID NO:4 or fragment thereof can provide a protective immune response in a subject against infection by *N. meningitidis* or *N. gonorrhoeae*.

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Both of these related bacteria infect mammalian subjects through binding of the bacteria to epithelial cells.

3.   That the following experiments were performed by me or under my direction and control.

4.   Hyperimmune antisera were generated in rabbits via standard protocols to the following immunogens: (a) the first 178 amino acids of Omp85 (SEQ ID NO:4), which is a sequence substantially conserved[1] in both Omp85 proteins of both *N. meningitidis* and *N. gonorrhoeae*; and (b) an unrelated antigen, bovine serum albumin (BSA). Normal rabbit serum (NRS) was used as the control. Fab fragments were prepared from all three antisera and added at 1 μg, 10 μg, or 100 μg per mL to wells containing a confluent layer of Chang conjunctival cells, which are standard representative mammalian epithelial cells. Approximately 2.5×10^5 bacteria (transparent *N. gonorrhoeae* strains MS11LOSA or FA19) were added to each well and allowed to adhere for 3 hours. Following fixation and immunogold/silver staining, the number of adherent gonococci was determined for 22 cells. The lowest and highest numbers were discarded and the average number of bacteria/cells determined. These data were then plotted in bar graph form.

5.   Exhibit A is a bar graph which illustrates the amount of bacterial cells ($\times 10^4$) present in each well after adherence, fixation, and staining. It is noted that Omp85-specific antibodies are able to bind to the surface of the bacteria and thereby interfere with the ability of the bacteria to adhere to the epithelial cells. It is necessary for the bacteria of *N. meningitidis* or *N. gonorrhoeae* to bind epithelial cells to initiate infection. Thus, these assay results demonstrate that the Omp85-specific antibodies

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[1]   SEQ ID NO:4 (*N. meningitidis*) differs from SEQ ID NO:2 (*N. gonorrhoeae*) at amino acid positions 82 (Gln or Leu, respectively), 89 (Glu or Val, respectively), and 90 (Arg or Cys, respectively).

generated to a fragment of SEQ ID NO: 4 can block the infection-initiating step. These assay results indicate that this polypeptide can be used to generate antibodies in a mammal, and that such antibodies can interfere with the process by which the bacteria infects the epithelial cells of the mammalian subject to cause disease. Thus, the polypeptides and fragments of this invention can mediate a protective immune response to infection of a mammal by the bacteria.
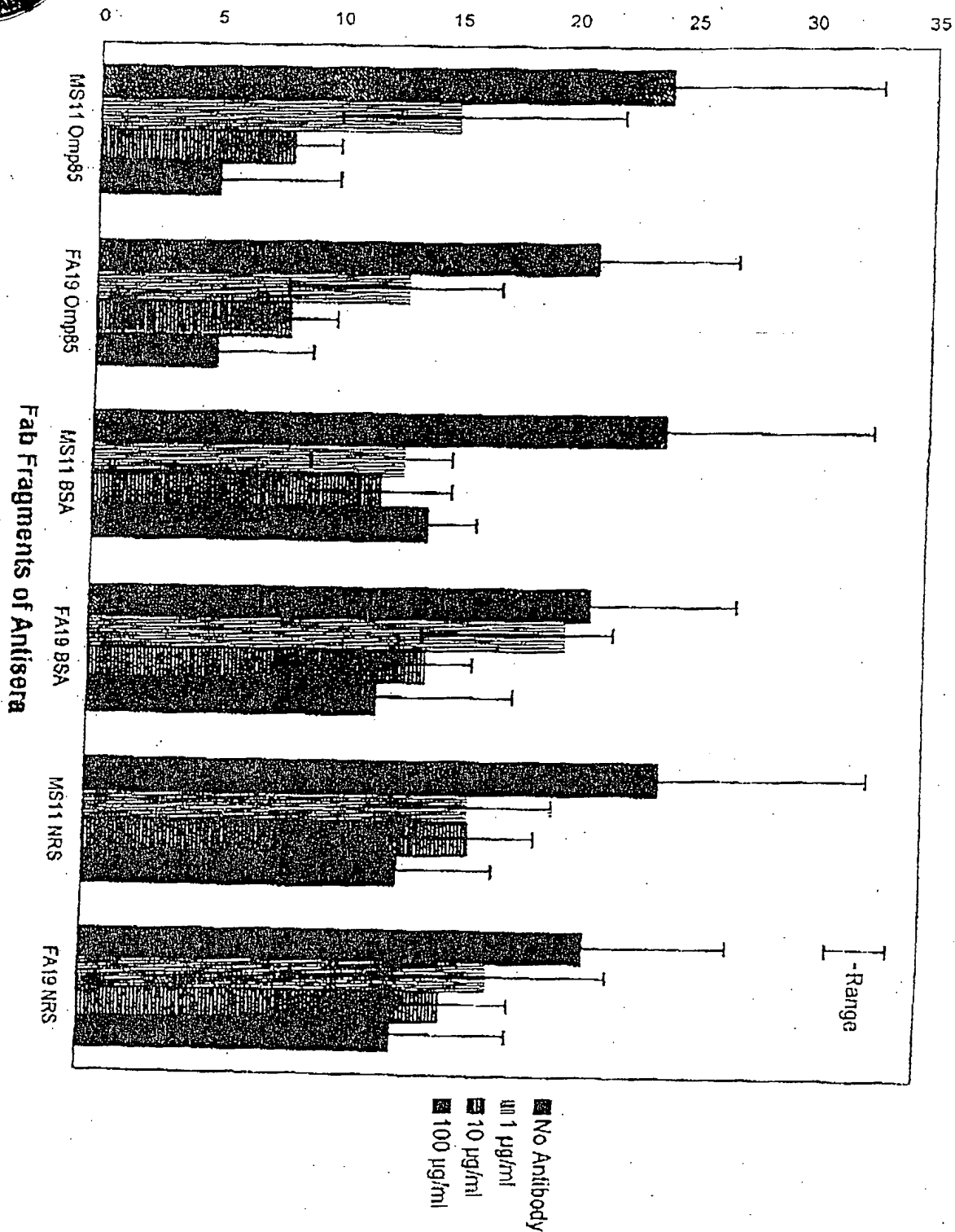
6.   I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 10/16/02   By: _____

                                        Ralph C. Judd, Ph.D.

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EXHIBIT A

Bacteria/Cell

Gonococcal Cell Adherence Assay

Fab Fragments of Antisera

MS11 Omp85
FA19 Omp85
MS11 BSA
FA19 BSA
MS11 NRS
FA19 NRS

0   5   10   15   20   25   30   35

- Range

No Antibody
1 µg/ml
10 µg/ml
100 µg/ml

In re Katz

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1641
	)
Ralph C. Judd *et al*	) Examiner: S. Devi
	)
Appln. No.: 09/177,039	) CERTIFICATE UNDER 37 CFR 1.8(a)
	) I hereby certify that this correspondence is being
Filed: October 22, 1998	) deposited with the United States Postal Service as first
	) class mail, postage prepaid, on the date indicated below
For: OMP85 PROTEINS OF	) in an envelope addressed to: Assistant Commissioner for
NEISSERIA GONORRHOEAE	) Patents, Washington, DC 20231
AND *NEISSERIA MENINGITIDIS,*	)
COMPOSITIONS CONTAINING	) Signature *C. Benedetto*
SAME AND METHODS OF USE	) Date _8-1-00_
THEREOF	

Assistant Commissioner for Patents
Washington, DC 20231

DECLARATION

Sir:

The undersigned, RALPH C. JUDD, residing at 316 Wickiup, Florence,

Montana 59833, a citizen of the United States, and D. SCOTT MANNING, residing at

2205 Westfield, Missoula, Montana 59801, a citizen of the United States, do declare

and state that:

1.   We are the named joint inventors of the subject matter claimed

in the above-referenced patent application.

2.   We understand that this Declaration is being submitted in the

above-identified application to traverse the Examiner's rejection in the Office Action

dated March 2, 2000 under 35 U.S.C. §102(a), and specifically to identify and

distinguish the inventors from the coauthors.

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3.   DENNIS K. RESCHKE [hereinafter COAUTHOR] is a named co-author, together with Declarants, D. SCOTT MANNING and RALPH C. JUDD [hereinafter INVENTORS], of D. S. Manning *et al*, Microbiol. Pathogen., 25:11-21 (July 1998).

4.   COAUTHOR is not an inventor of the subject matter of the above-mentioned application. As a graduate student in Dr. Judd's laboratory at the University of Montana, the assignee of the above-identified application, COAUTHOR performed technical experiments at Dr. Judd's direction and under Dr. Judd's supervision.

5.   INVENTORS did conceive and cause to be reduced to practice in the United States of America, the invention claimed in the subject application, as it relates to the Omp85 proteins of N. gonorrhoeae and N. meningitidis and its uses, prior to the effective reference date of D. S. Manning *et al*, Microbiol. Pathogen., 25:11-21 (July 1998).

7.   All statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true; these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

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United States Code and that such willful false statements may jeopardize the validity of

the application or any patent issuing thereon.

Date: 7/31/00   By: _____
                          Ralph C. Judd

Date: 7/31/00   By: _____
                          D. Scott Manning

Omp85 comparisons

Protein sequences used :

Species	Strain	Genbank accession number
N.gonorrhoeae	FA1090	AAW90419
N.gonorrhoeae	FA19	AAC17600 (SEQ ID NO: 2 of appln)
N.meningitidis B	HH	AAC17599 (SEQ ID NO: 4 of appln)
N.meningitidis B	MC58	NP_273240
N.meningitidis A	Z2491	NP_282936

Identity percentage (computed with ClustalW program) :

	FA19	HH	MC58	Z2491
FA1090	99	95	95	95
FA19		95	95	95
HH			99	99
MC58				99

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                    *          20          *          40          *          60
OMP85_MC58 : MKLKQIASALMMLGISPLALADFTIQDIRVEGLQRTEPSTVFNYLPVKVGDTYNDTHGSA :  60
OMP85_Z249 : MKLKQIASALMVLGISPLALADFTIQDIRVEGLQRTEPSTVFNYLPVKVGDTYNDTHGSA :  60
OMP85_HH   : MKLKQIASALMMLGISPLAEADFTIQDIRVEGLQRTEPSTVFNYLPVKVGDTYNDTHGSA :  60
OMP85_FA10 : MKLKQIASALMMLGISPLAEADFTIQDIRVEGLQRTEPSTVFNYLPVKVGDTYNDTHGSA :  60
OMP85_FA19 : MKLKQIASALMMLGISPLAEADFTIQDIRVEGLQRTEPSTVFNYLPVKVGDTYNDTHGSA :  60


                    *          80          *         100          *         120
OMP85_MC58 : IIKSLYATGFFDDVRVETADGQLLLTVIERPTIGSLNITGAKMLQNDAIKKNLESFGLAQ : 120
OMP85_Z249 : IIKSLYATGFFDDVRVETADGQLLLTVIERPTIGSLNITGAKMLQNDAIKKNLESFGLAQ : 120
OMP85_HH   : IIKSLYATGFFDDVRVETADGQLLLTVIERPTIGSLNITGAKMLQNDAIKKNLESFGLAQ : 120
OMP85_FA10 : IIKSLYATGFFDDVRVETADGQLLLTVIERPTIGSLNITGAKMLQNDAIKKNLESFGLAQ : 120
OMP85_FA19 : IIKSLYATGFFDDVRVETADGLLLLTVIVCPTIGSLNITGAKMLQNDAIKKNLESFGLAQ : 120


                    *         140          *         160          *         180
OMP85_MC58 : SQYFNQATLNQAVAGLKEEYLGRGKLNIQITPKVTKLARNRVDIDITIDEGKSAKITDIE : 180
OMP85_Z249 : SQYFNQATLNQAVAGLKEEYLGRGKLNIQITPKVTKLARNRVDIDITIDEGKSAKITDIE : 180
OMP85_HH   : SQYFNQATLNQAVAGLKEEYLGRGKLNIQITPKVTKLARNRVDIDITIDEGKSAKITDIE : 180
OMP85_FA10 : SQYFNQATLNQAVAGLKEEYLGRGKLNIQITPKVTKLARNRVDIDITIDEGKSAKITDIE : 180
OMP85_FA19 : SQYFNQATLNQAVAGLKEEYLGRGKLNIQITPKVTKLARNRVDIDITIDEGKSAKITDIE : 180


                    *         200          *         220          *         240
OMP85_MC58 : FEGNQVYSDRKLMRQMSLTEGGIWTWLTRSNQFNEQKFAQDMEKVTDFYQNNGYFDFRIL : 240
OMP85_Z249 : FEGNQVYSDRKLMRQMSLTEGGIWTWLTRSNQFNEQKFAQDMEKVTDFYQNNGYFDFRIL : 240
OMP85_HH   : FEGNQVYSDRKLMRQMSLTEGGIWTWLTRSNQFNEQKFAQDMEKVTDFYQNNGYFDFRIL : 240
OMP85_FA10 : FEGNQVYSDRKLMRQMSLTEGGIWTWLTRSDRFDRQKFAQDMEKVTDFYQNNGYFDFRIL : 240
OMP85_FA19 : FEGNQVYSDRKLMRQMSLTEGGIWTWLTRSDRFDRQKFAQDMEKVTDFYQNNGYFDFRIL : 240
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                       *         260         *         280         *         300
OMP85_MC58 : DTDIQTNEDKTKQTIKITVHEGGRFRWGKVSIEGDTNEVPKAELEKLLTMKPGKWYERQQ : 300
OMP85_Z249 : DTDIQTNEDKTKQTIKITVHEGGRFRWGKVSIEGDTNEVPKAELEKLLTMKPGKWYERQQ : 300
OMP85_HH   : DTDIQTNEDKTKQTIKITVHEGGRFRWGKVSIEGDTNEVPKAELEKLLTMKPGKWYERQQ : 300
OMP85_FA10 : DTDIQTNEDKTRQTIKITVHEGGRFRWGKVSIEGDTNEVPKAELEKLLTMKPGKWYERQQ : 300
OMP85_FA19 : DTDIQTNEDKTRQTIKITVHEGGRFRWGKVSIEGDTNEVPKAELEKLLTMKPGKWYERQQ : 300


                       *         320         *         340         *         360
OMP85_MC58 : MTAVLGEIQNRMGSAGYAYSEISVQPLPNAETKTVDFVLHIEPGRKIYVNEIHITGNNKT : 360
OMP85_Z249 : MTAVLGEIQNRMGSAGYAYSEISVQPLPNAETKTVDFVLHIEPGRKIYVNEIHITGNNKT : 360
OMP85_HH   : MTAVLGEIQNRMGSAGYAYSEISVQPLPNAETKTVDFVLHIEPGRKIYVNEIHITGNNKT : 360
OMP85_FA10 : MTAVLGEIQNRMGSAGYAYSEISVQPLPNAGTKTVDFVLHIEPGRKIYVNEIHITGNNKT : 360
OMP85_FA19 : MTAVLGEIQNRMGSAGYAYSEISVQPLPNAGTKTVDFVLHIEPGRKIYVNEIHITGNNKT : 360


                       *         380         *         400         *         420
OMP85_MC58 : RDEVVRRELRQMESAPYDTSKLQRSKERVELLGYFDNVQFDAVPLAGTPDKVDLNMSLTE : 420
OMP85_Z249 : RDEVVRRELRQMESAPYDTSKLQRSKERVELLGYFDNVQFDAVPLAGTPDKVDLNMSLTE : 420
OMP85_HH   : RDEVVRRELRQMESAPYDTSKLQRSKERVELLGYFDNVQFDAVPLAGTPDKVDLNMSLTE : 420
OMP85_FA10 : RDEVVRRELRQMESAPYDTSKLQRSKERVELLGYFDNVQFDAVPLAGTPDKVDLNMSLTE : 420
OMP85_FA19 : RDEVVRRELRQMESAPYDTSKLQRSKERVELLGYFDNVQFDAVPLAGTPDKVDLNMSLTE : 420


                       *         440         *         460         *         480
OMP85_MC58 : RSTGSLDLSAGWVQDTGLVMSAGVSQDNLFGTGKSAALRASRSKTTLNGSLSFTDPYFTA : 480
OMP85_Z249 : RSTGSLDLSAGWVQDTGLVMSAGVSQDNLFGTGKSAALRASRSKTTLNGSLSFTDPYFTA : 480
OMP85_HH   : RSTGSLDLSAGWVQDTGLVMSAGVSQDNLFGTGKSAALRASRSKTTLNGSLSFTDPYFTA : 480
OMP85_FA10 : RSTGSLDLSAGWVQDTGLVMSAGVSQDNLFGTGKSAALRASRSKTTLNGSLSFTDPYFTA : 480
OMP85_FA19 : RSTGSLDLSAGWVQDTGLVMSAGVSQDNLFGTGKSAALRASRSKTTLNGSLSFTDPYFTA : 480


                       *         500         *         520         *         540
OMP85_MC58 : DGVSLGYDVYGKAFDPRKASTSIKQYKTTTAGAGIRMSVPVTEYDRVNFGLVAEHLTVNT : 540
OMP85_Z249 : DGVSLGYDVYGKAFDPRKASTSIKQYKTTTAGAGIRMSVPVTEYDRVNFGLVAEHLTVNT : 540
OMP85_HH   : DGVSLGYDVYGKAFDPRKASTSIKQYKTTTAGAGIRMSVPVTEYDRVNFGLVAEHLTVNT : 540
OMP85_FA10 : DGVSLGYDIYGKAFDPRKASTSVKQYKTTTAGGGVRMGIPVTEYDRVNFGLAAEHLTVNT : 540
OMP85_FA19 : DGVSLGYDIYGKAFDPRKASTSVKQYKTTTAGGGVRMGIPVTEYDRVNFGLAAEHLTVNT : 540


                       *         560         *         580         *         600
OMP85_MC58 : YNKAPKHYADFIKKYGKTDGTDGSFKGWLYKGTVGWGRNKTDSALWPTRGYLTGVNAEIA : 600
OMP85_Z249 : YNKAPKHYADFIKKYGKTDGTDGSFKGWLYKGTVGWGRNKTDSALWPTRGYLTGVNAEIA : 600
OMP85_HH   : YNKAPKHYADFIKKYGKTDGTDGSFKGWLYKGTVGWGRNKTDSALWPTRGYLTGVNAEIA : 600
OMP85_FA10 : YNKAPKRYADFIRKYGKTDGADGSFKGILYKGTVGWGRNKTDSASWPTRGYLTGVNAEIA : 600
OMP85_FA19 : YNKAPKRYADFIKQYGKTDGADGSFKGILYKGTVGWGRNKTDSALWPTRGYLTGVNAEIA : 600


                       *         620         *         640         *         660
OMP85_MC58 : LPGSKLQYYSATHNQTWFFPLSKTFTLMLGGEVGIAGGYGRTKEIPFFENFYGGGLGSVR : 660
OMP85_Z249 : LPGSKLQYYSATHNQTWFFPLSKTFTLMLGGEVGIAGGYGRTKEIPFFENFYGGGLGSVR : 660
OMP85_HH   : LPGSKLQYYSATHNQTWFFPLSKTFTLMLGGEVGIAGGYGRTKEIPFFENFYGGGLGSVR : 660
OMP85_FA10 : LPGSKLQYYSATHNQTWFFPLSKTFTLMLGGEVGIAGGYGRTKEIPFFENFYGGGLGSVR : 660
OMP85_FA19 : LPGSKLQYYSATHNQTWFFPLSKTFTLMLGGEVGIAGGYGRTKEIPFFENFYGGGLGSVR : 660
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                      *          680         *          700         *          720
OMP85_MC58 : GYESGTLGPKVYDEYGEKISYGGNKKANVSAELLFPMPGAKDARTVRLSLFADAGSVWDG : 720
OMP85_Z249 : GYESGTLGPKVYDEYGEKISYGGNKKANVSAELLFPMPGAKDARTVRLSLFADAGSVWDG : 720
OMP85_HH   : GYESGTLGPKVYDEYGEKISYGGNKKANVSAELLFPMPGAKDARTVRLSLFADAGSVWDG : 720
OMP85_FA10 : GYESGTLGPKVYDEYGEKISYGGNKKANVSAELLFPMPGAKDARTVRLSLFADAGSVWDG : 720
OMP85_FA19 : GYESGTLGPKVYDEYGEKISYGGNKKANVSAELLFPMPGAKDARTVRLSLFADAGSVWDG : 720


                      *          740         *          760         *          780
OMP85_MC58 : KTYDDNSSATGGRVQNIYGAGNTHKSTFTNELRYSAGGAVTWLSPLGPMKFSYAYPLKK : 780
OMP85_Z249 : KTYDDNSSATGGRVQNIYGAGNTHKSTFTNELRYSAGGAVTWLSPLGPMKFSYAYPLKK : 780
OMP85_HH   : KTYDDNSSATGGRVQNIYGAGNTHKSTFTNELRYSAGGAVTWLSPLGPMKFRYAYPLKK : 780
OMP85_FA10 : RTY----TAAENGNNKSVY-SENAHKSTFTNELRYSAGGAVTWLSPLGPMKFSYAYPLKK : 775
OMP85_FA19 : RTY----TAAENGNNKSVY-SENAHKSTFTNELRYSAGGAVTWLSPLGPMKFIYAYPLKK : 775


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OMP85_MC58 : KPEDEIQRFQFQLGTTF : 797
OMP85_Z249 : KPEDEIQRFQFQLGTTF : 797
OMP85_HH   : KPEDEIQRFQFQLGTTF : 797
OMP85_FA10 : KPEDEIQRFQFQLGTTF : 792
OMP85_FA19 : KPEDEIQRFQFQLGTTF : 792
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